Amendments

In the Claims:

Please cancel claims 30, 54, 74, 91 and 106. Please amend claims 29, 44, 47, 51, 56, 65, 68, 71, 76, 82, 85, 88, 93, 101, 108, 114, 116, 118, 120, 122, 123, 125, 128 and 129 as follows.

1-19. (Canceled).

20. (Previously Presented) A compound of formula (I)

$$\begin{array}{c|c}
R_4 & R_5 \\
N & R_1 \\
N & R_{10}
\end{array}$$

$$\begin{array}{c|c}
(R_3)_0 \\
R_2
\end{array}$$

$$\begin{array}{c|c}
(I)
\end{array}$$

wherein

R is a halogen atom or a C₁₋₄ alkyl group; R₁ is hydrogen or a C₁₋₄ alkyl group;

 R_2 is hydrogen, a C_{1-4} alkyl, C_{2-6} alkenyl or a C_{3-7} cycloalkyl group; or R_1 and R₂ together with nitrogen and carbon atom to which they are attached respectively are a 5-6 membered heterocyclic group;

R₃ is a trifluoromethyl, a C₁₋₄ alkyl, a C₁₋₄ alkoxy, a trifluoromethoxy, or a halogen group;

 R_4 is hydrogen, a $(CH_2)_qR_7$ or a $(CH_2)_rCO/(CH_2)_pR_7$ group;

R₅ is hydrogen, a C₁₋₄ alkyl or a COR₆ group;

R_s is hydrogen, hydroxy, amino, methylamino, dimethylamino, a 5 membered heteroaryl group containing 1 to 3 heteroatoms selected from oxygen, sulphur and nitrogen or a 6 membered heteroaryl|group containing 1 to 3 nitrogen atoms:

R₇ is hydrogen, hydroxy or NR₈R₉ wherein R₈ and R₉ are independently hydrogen or C₁₋₄ alkyl optionally substituted by hydroxy, or by amino;

R₁₀ is hydrogen, a C₁₋₄ alkyl I group or

R₁₀ together with R₂ is a C₃₋₇ cycloalkyl group;

m is zero or an integer from 1 to 3; n is zero or an integer from 1 to 3; both p and r are independently zero or an integer from 1 to 4; q is an integer from 1 to 4; provided that , when R_1 and R_2 together with nitrogen and carbon atom to which they are attached respectively are a 5 to 6 membered heterocyclic group, i) m is 1 or 2; ii) when m is 1, R is not fluorine and iii) when m is 2, the two substituents R are not both fluorine, or a pharmaceutically acceptable salt or solvate thereof.

- 21. (Previously Presented) A compound as claimed in claim 20 wherein n is 2 and R₃ is trifluoromethyl both at the 3 and 5 position.
- 22. (Previously Presented) A compound as claimed in claim 20 wherein R is selected independently from halogen or a C₁₋₄ alkyl group and m is 1 or 2.
- 23. (Previously Presented) A compound as claimed in claim 20 wherein m is 2, R is selected independently from halogen or methyl group at 2 or 4 position.
- 24. (Previously Presented) A compound as claimed in claim 20 wherein R_s is hydrogen or a methyl group.
- 25. (Previously Presented) A compound as claimed in claim 20 wherein R₁ is hydrogen or a methyl group.
- 26. (Previously Presented) A compound as claimed in claim 20 wherein R_4 is hydrogen, a $(CH_2)_rCO(CH_2)_pR_7$ or $CH_2)_qR_7$ group, wherein R_7 represents an amine, both p and r are independently zero or 1; and q is 1 or 2.
- 27. (Previously Presented) A compound as claimed in claim 20 wherein R is selected independently from halogen or methyl, R₃ is trifluoromethyl both

at the 3 and 5 position, R_1 is hydrogen or methyl, R_2 is hydrogen, methyl, 2-propenyl or a cyclopropyl group or together with R_1 is a 3,6-dihydro-2H-pyridin-1-yl, a piperidin-1-yl or a pyrrolidin-1-yl group, R_{10} represents hydrogen, a methyl or R_{10} together with R_2 is a cyclopropyl group, R_4 is hydrogen, an aminoacetyl or amino ethyl group and R_5 is hydrogen or a methyl group.

- 28. (Previously Presented) A compound as claimed in claim 20 wherein R is selected independently from halogen or methyl and m is 2, R_3 is trifluoromethyl both at the 3 and 5 position, R_1 and R_2 are independently hydrogen or methyl, R_4 is hydrogen and R_5 is hydrogen.
- 29. (Currently Amended) A compound selected from:
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2-isopropyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-3-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2,4-difluoro-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide;
- 2-(4-fluoro-phenyl)- piperazine-1-carboxylic acid (3,4-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-phenyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methylamide;
- 2-(2,4-dichloro-phenyl)-piperazine-1-carb oxylic acid (3,5-bistrifluoro methyl-benzyl)-methyl-amide;
- 2-(3,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro methyl-benzyl)-methyl-amide;

- 2-(4-fluoro-2-methyl-phenyl)-3-methyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2-methyl-4-fluoro-phenyl)-6-methyl- piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phonyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phonyl)ethyl]-methyl-amide;
- 4-(2-amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(S)-(4-fluore-2-methyl-phenyl) 4-(piperidine-4-carbonyl) piperazine 1-carboxylic acid (3,5-bis-trifluoremethyl-benzyl) methyl-amide;
- 4-(2-amino-ethyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(1-3,5-bis-trifluoromethyl-phenyl)-cyclopropy]-methyl-amide;
- [2-(3,5-bis-trifluoromethyl-phenyl)-pyrrolidin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
- [2-(3,5-bis-trifluoromethyl-phenyl)-3,6-dihydro-*2H*-pyridyn-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-i-yl]-methanone;
- 2-(3,5-bis-trifluoromethyl-phenyl)-piperidih-1-yl]-[2-(\$)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-but-3-enyl]-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propyl]-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(3,5-bis-trifluoromethyl-phenyl)-cyclopropyl-methyl]-methyl-amide; and enantiomers, pharmaceutically acceptable salts, and solvates thereof.

30. (Canceled.)

31. (Previously Presented) 4-(2-amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide hydrochloride.

- 32. (Previously Presented) 2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide methanesulphonate.
- 33. (Previously Presented) 2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide acetate.
- 34. (Previously Presented) A pharmaceutical composition comprising a compound as claimed in claim 20 in admixture with one or more physiologically acceptable carriers or excipients.

35-37. (Cancelled.)

38. (Previously Presented) A process (A) for the preparation of a compound as claimed in claim 20, wherein R_4 is hydrogen or a $(CH_2)_qR_7$ group, provided that when R_5 is a C_{1-4} alkyl or a COR_6 group, R_5 is not in the 3 position of the piperazine ring, which comprises reduction of a compound of formula (II), wherein $(R_4)_a$ is hydrogen or a suitable nitrogen protecting group or $(R_4)_a$ is a $(CH_2)_qR_7$ group or protecting derivatives thereof; or

$$(R_4)_{\bullet}$$
 N R_5 R_{10} $(R_3)_n$ R_{20} $(R_1)_m$

a process (B) for the preparation of a compound as claimed in claim 20, wherein R_4 is hydrogen or a $(CH_2)_rCO(CH_2)_pR_7$ group which comprises the reaction of a compound of formula (VIII), wherein $(R_4)_b$ represents a nitrogen protecting group or $(R_4)_b$ is $(CH_2)_rCO(CH_2)_pR_7$ or a protecting group thereof with triphosgene and an organic base followed by addition of the amine (V)

$$(R_d)_b$$
 NH
 R_5
 R_1
 R_{10}
 R_{10}
 R_{10}
 R_{10}
 R_{10}
 R_{10}
 R_{10}
 R_{10}
 R_{10}
 R_{10}

followed where necessary or desired by one or more of the following steps:

- (i) removal of any protecting group;
- (ii) isolation of the compound as salt thereof;
- (iii) separation of a compound of formula (i) or derivative thereof into the enantiomers thereof.
- 39. (Previously Presented) A method for the treatment of a depressive state in a mammal comprising administering to said mammal an effective amount of a compound of formula (I):

$$\begin{array}{c|c} R_4 & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ &$$

wherein:

R is a halogen atom or a C₁₋₄ alkyl group;

R₁ is hydrogen or a C₁₋₄ alkyl group;

 R_2 is hydrogen, a C_{1-4} alkyl, C_{2-6} alkenyl or a C_{3-7} cycloalkyl group; or R_1 and R_2 together with nitrogen and carbon atom to which they are attached respectively represent a 5-6 membered heterocyclic group;

 R_3 is a trifluoromethyl, a C_{1-4} alkyl, a C_{1-4} alkoxy, a trifluoromethoxy or a halogen group;

R₄ is hydrogen, a (CH₂)_qR₇ or a (CH₂) CO(CH₂)_pR₇ group;

R₅ is hydrogen, a C₁₋₄ alkyl or a COR₆ group;

7 of 3

R₆ is hydrogen, hydroxy, amino, methylamino, dimethylamino a 5 membered heteroaryl group containing 1 to 3 heteroatoms selected from oxygen, sulphur and nitrogen or a 6 membered heteroaryl group containing 1 to 3 nitrogen atoms;

R₇ is hydrogen, hydroxy or NR₈R₉ wherein R₈ and R₉ represent independently hydrogen or C₁₋₄ alkyl optionally substituted by hydroxy or by amino;

 R_{10} is hydrogen, a C_{1-4} alkyl group or R_{10} together with R_2 represents a C_{3-7} cycloalkyl group;

m is zero or an integer from 1 to 3;

n is zero or an integer from 1 to 3;

both p and r are independently zero of an integer from 1 to 4;

q is an integer from 1 to 4;

provided that, when R₁ and R₂ together with nitrogen and carbon atom to which they are attached respectively represent a 5 to 6 membered heterocyclic group,

- i) m is 1 or 2;
- ii) when m is 1, R is not fluorine and
- iii) when m is 2, the two substituents R are not both fluorine, or a pharmaceutically acceptable salt or solvate thereof.
- 40. (Previously Presented) The method according to claim 39, wherein said mammal is man.
- 41. (Previously Presented) The method according to claim 39, wherein said depressive state is selected from the group consisting of bipolar depression, unipolar depression, single major depressive episodes, recurrent major depressive episodes, dysthymic disorder, neurotic depression, social phobia, dementia of Alzheimer's type, vascular dementia with depressed mood, mood disorders induced by alcohol, mood disorders induced by amphetamines, mood disorders induced by cocaine, mood disorders induced by hallucinogens, mood disorders induced by inhalants, mood disorders

induced by opioids, mood disorders induced by phencyclidine, mood disorders induced by sedatives, mood disorders induced by hypnotics, mood disorders induced by anxiolytics and schizoaffective disorder of the depressed type.

- 42. (Previously Presented) The method according to claim 39, wherein said depressive state is selected from the group consisting of bipolar depression and unipolar depression.
- 43. (Previously Presented) The method according to claim 39, further comprising administering an effective amount of a serotonin reuptake inhibitor.
- 44. (Currently Amended) The method according to claim 43, wherein said serotonin reuptake inhibitor is selected from the group consisting of fluoxetine, cialopram citalopram, femoxetine, fluoxamine, paroxetine, indalpine, sertraline, zimeldine.
- 45. (Previously Presented) The method according to claim 39, further comprising administering an effective amount of a dopaminergic antidepressant.
- 46. (Previously Presented) The method according to claim 45, wherein said dopaminergic antidepressant is selected from the group consisting of buproprion and amineptine.
- 47. (Currently Amended) A method for the treatment of a depressive state in a mammal comprising administering to said mammal an effective amount of a compound selected from the group consisting of
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2-Isopropyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-Fluoro-3-methyl-phenyl)-piperazine-|1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;

- 2-(2,4-Difluoro-phenyl)-piperazine-1-carb pxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide;
- 2-(4-Fluoro-phenyl)- piperazine-1-carboxylic acid (3,4-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-Phenyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methylamide;
- 2-(2,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro-methyl-benzyl)-methyl-amide;
- 2-(3,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro-methyl-benzyl)-methyl-amide;
- 2-(4-Fluoro-2-methyl-phenyl)-3-methyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2-Methyl-4-Fluoro-phenyl)-6-Methyl- piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro 2 methyl-phenyl)-piperazine 1 carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)othyl] methyl-amide;
- 4-(2-Amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzy|)-methyl-amide;
- 2 (S) (1 Fluoro-2-methyl-phenyl) 1 (piperidine 1 carbonyl)-piperazine 1 carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 4-(2-Amino-ethyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(1-3,5-bis-trifluoromethyl-phenyl)-cyclopropy|]-methyl-amide;
- [2-(3,5-Bis-trifluoromethyl-phenyl)-pyrrol(din-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
- [2-(3,5-Bis-trifluoromethyl-phenyl)-3,6-dihydro-2H-pyridyn-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
- 2-(3,5-Bis-trifluoromethyl-phenyl)-piperid(n-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;

- 2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-but-3-enyl]-methyl-amide;
- 2-(4-Fluoro-2-methyl-phenyl)-piperazine-||1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propyl]-methyl-amide;
- 2-(4-Fluoro-2-methyl-phenyl)-piperazine-[1-carboxylic acid [(3,5-bis-trifluoromethyl-phenyl)-cyclopropy -methyl]-methyl-amide; or an enantiomer, or pharmaceutically acceptable salt or solvate thereof.
- 48. (Previously Presented) The method according to claim 47, wherein said mammal is man.
- 49. (Previously Presented) The method according to claim 47, wherein said depressive state is selected from the group consisting of bipolar depression and unipolar depression.
- 50. (Previously Presented) The method according to claim 47, further comprising administering an effective amount of a serotonin reuptake inhibitor.
- 51. (Currently Amended) The method according to claim 50, wherein said serotonin reuptake inhibitor is selected from the group consisting of fluoxetine, cialopram citalopram, femoxetine, fluvoxamine, paroxetine, indalpine, sertraline, zimeldine.
- 52. (Previously Presented) The method according to claim 47, further comprising administering an effective amount of a dopaminergic antidepressant.
- 53. (Previously Presented) The method according to claim 52, wherein said dopaminergic antidepressant is selected from the group consisting of buproprion and amineptine.
- 54. (Cancelled.)

- 55. (Previously Presented) A method for the treatment of a depressive state in a mammal comprising administering to said mammal an effective amount of 4-(2-Amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide hydrochloride.
- 56. (Currently Amended) A method for the treatment of a depressive state in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2 methyl phenyl) piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl phenyl) ethyl] methyl-amide 2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-ethyl] methyl-amide or an enantiomer or pharmaceutically acceptable salt or solvate thereof.
- 57. (Previously Presented) The method according to claim 56, wherein said depressive state is selected from the group consisting of bipolar depression and unipolar depression.
- 58. (Previously Presented) A method for the treatment of a depressive state in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl] methyl-amide methansulphonate.
- 59. (Previously Presented) The method according to claim 58, wherein said depressive state is selected from the group consisting of bipolar depression and unipolar depression.
- 60. (Previously Presented) A method for the treatment of a depressive state in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]+methyl-amide acetate.

- 61. (Previously Presented) The method according to claim 60, wherein said depressive state is selected from the group consisting of bipolar depression and unipolar depression.
- 62. (Previously Presented) A method for the treatment of anxiety in a mammal comprising administering to said mammal an effective amount of a compound of formula (I):

$$R_4$$
 N R_5 R_1 R_{10} R_{10} R_{10} R_{10} R_{10} R_{10} R_{10}

wherein:

R is a halogen atom or a C₁₋₄ alkyl group;

R₁ is hydrogen or a C₁₋₄ alkyl group;

 R_2 is hydrogen, a C_{1-4} alkyl, C_{2-6} alkenyl or a C_{3-7} cycloalkyl group; or R_1 and R_2 together with nitrogen and carbon atom to which they are attached respectively represent a 5-6 membered heterocyclic group;

R₃ is a trifluoromethyl, a C₁₋₄ alkyl, a C₁₋₄ alkoxy, a trifluoromethoxy or a halogen group;

 R_4 is hydrogen, a $(CH_2)_qR_7$ or a $(CH_2)_pCO(CH_2)_pR_7$ group;

R_s is hydrogen, a C₁₋₄ alkyl or a COR₆ group;

R₆ is hydrogen, hydroxy, amino, methylamino, dimethylamino a 5 membered heteroaryl group containing 1 to 3 heteroatoms selected from oxygen, sulphur and nitrogen or a 6 membered heteroaryl group containing 1 to 3 nitrogen atoms;

 R_7 is hydrogen, hydroxy or NR_8R_9 wherein R_8 and R_9 represent independently hydrogen or $C_{1,4}$ alkyl optionally substituted by hydroxy or by amino;

R₁₀ is hydrogen, a C₁₋₄ alkyl group or R₁₀ together with R₂ represents a C₃₋₇ cycloalkyl group;
m is zero or an integer from 1 to 3;
both p and r are independently zero or an integer from 1 to 4;
q is an integer from 1 to 4;
provided that, when R₁ and R₂ together with nitrogen and carbon atom to which they are attached respectively represent a 5 to 6 membered heterocyclic group,

- i) m is 1 or 2;
- ii) when m is 1, R is not fluorine and
- iii) when m is 2, the two substituents R are not both fluorine, or a pharmaceutically acceptable salt or solvate thereof.
- 63. (Previously Presented) The method according to claim 62, wherein said mammal is a human.
- 64. (Previously Presented) The method according to claim 62, further comprising administering an effective amount of a serotonin reuptake inhibitor.
- 65. (Currently Amended) The method according to claim 64, wherein said serotonin reuptake inhibitor is selected from the group consisting of fluoxetine, cialopram citalopram, femoxetine, fluvoxamine, paroxetine, indalpine, sertraline, zimeldine.
- 66. (Previously Presented) The method according to claim 62, further comprising administering an effective amount of a dopaminergic antidepressant.
- 67. (Previously Presented) The method according to claim 66, wherein said dopaminergic antidepressant is selected from the group consisting of buproprion and amineptine.

PI3806USW

- 68. (Currently Amended) A method for the treatment of anxiety in a mammal comprising administering to said mammal an effective amount of a compound selected from the group consisting of
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoromethyl-benzyl)-methyl-amide;
- 2-(2-Isopropyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethylbenzyl)-methyl-amide;
- 2-(4-Fluoro-3-methyl-phenyl)-piperazine-||1-carboxylic acid (3,5-bistrifluoromethyl-benzyl)-methyl-amide;
- 2-(2,4-Difluoro-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethylbenzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bistrifluoromethyl-phenyl)ethyl]-methyl-amide;
- 2-(4-Fluoro-phenyl)- piperazine-1-carboxylic acid (3,4-bis-trifluoromethylbenzyl)-methyl-amide;
- 2-Phenyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methylamide;
- 2-(2,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro-methylbenzyl)-methyl-amide;
- 2-(3,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro-methylbenzyl)-methyl-amide;
- 2-(4-Fluoro-2-methyl-phenyl)-3-methyl-piperazine-1-carboxylic acid (3,5-bistrifluoromethyl-benzyl)-methyl-amide;
- 2-(2-Methyl-4-Fluoro-phenyl)-6-Methyl- piperazine-1-carboxylic acid (3,5-bistrifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phonyl)-piperazine-1-carboxylic acid [1-(3,5-bistrifluoromethyl-phenyl)ethyl]-methyl-amide;
- 4-(2-Amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(S)-(4-Fluoro-2-methyl-phonyl) 1 (piperidine 4-carbonyl)-piperazine-1carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 4-(2-Amino-ethyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;

- 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(1-3,5-bis-trifluoromethyl-phenyl)-cyclopropy]-methyl-amide;
- [2-(3,5-Bis-trifluoromethyl-phenyl)-pyrrolidin-1-yl]-[2-(\$)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
- [2-(3,5-Bis-trifluoromethyl-phenyl)-3,6-dillydro-*2H*-pyridyn-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-[1-yl]-methanone;
- 2-(3,5-Bis-trifluoromethyl-phenyl)-piperidin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
- 2-(4-Fluoro-2-methyl-phenyl)-piperazine 1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-but-3-enyl] methyl-amide;
- 2-(4-Fluoro-2-methyl-phenyl)-piperazine-il-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propyl]-methyl-amide;
- 2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(3,5-bis-trifluoromethyl-phenyl)-cyclopropyl-methyl]-methyl-amide; or an enantiomer, or pharmaceutically acceptable salt or solvate thereof.
- 69. (Previously Presented) The method according to claim 68, wherein said mammal is a human.
- 70. (Previously Presented) The method according to claim 68, further comprising administering an effective amount of a serotonin reuptake inhibitor.
- 71. (Currently Amended) The method according to claim 70, wherein said serotonin reuptake inhibitor is selected from the group consisting of fluoxetine, cialopram citalopram, femoxetine, fluoxamine, paroxetine, indalpine, sertraline, zimeldine.
- 72. (Previously Presented) The method according to claim 68, further comprising administering an effective amount of a dopaminergic antidepressant.

- 73. (Previously Presented) The method according to claim 72, wherein said dopaminergic antidepressant is selected from the group consisting of buproprion and amineptine.
- 74. (Cancelled.)
- 75. (Previously Presented) A method for the treatment of anxiety in a mammal comprising administering to said mammal an effective amount of 4-(2-Amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide hydrochloride.
- 76. (Currently Amended) A method for the treatment of anxiety in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl) piperazine 1 carboxylic acid [1-(R) (3,5-bis-trifluoromethyl-phenyl) othyl] methyl-amide 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide or an enantiomer or pharmaceutically acceptable salt or solvate thereof.
- 77. (Previously Presented) A method for the treatment of anxiety in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide methansulphonate.
- 78. (Previously Presented) A method for the treatment of anxiety in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide acetate.

79. (Previously Presented) A method for the treatment of a panic disorder in a mammal comprising administering to said mammal an effective amount of a compound of formula (I):

$$R_4$$
 N R_5 R_1 R_{10} R_{20} R_{10} R_{20} R_{20}

wherein:

R is a halogen atom or a C₁₋₄ alkyl group;

R₁ is hydrogen or a C_{1.4} alkyl group;

 R_2 is hydrogen, a C_{1-4} alkyl, C_{2-6} alkerlyl or a C_{3-7} cycloalkyl group; or R_1 and R_2 together with nitrogen and carbon atom to which they are attached respectively represent a 5-6 membered heterocyclic group;

R₃ is a trifluoromethyl, a C₁₋₄ alkyl, a G₁₋₄ alkoxy, a trifluoromethoxy or a halogen group;

 R_4 is hydrogen, a $(CH_2)_qR_7$ or a $(CH_2)_pCO(CH_2)_pR_7$ group;

R₅ is hydrogen, a C₁₋₄ alkyl or a COR₆ group;

R₆ is hydrogen, hydroxy, amino, methylamino, dimethylamino a 5 membered heteroaryl group containing 1 to 3 heteroatoms selected from oxygen, sulphur and nitrogen or a 6 membered heteroaryl group containing 1 to 3 nitrogen atoms;

 R_7 is hydrogen, hydroxy or NR_8R_9 wherein R_8 and R_9 represent independently hydrogen or C_{1-4} alkyl optionally substituted by hydroxy or by amino;

 R_{10} is hydrogen, a C_{1-4} alkyl group or R_{10} together with R_2 represents a C_{3-7} cycloalkyl group;

m is zero or an integer from 1 to 3;

n is zero or an integer from 1 to 3;

both p and r are independently zero or an integer from 1 to 4;

q is an integer from 1 to 4; provided that, when R_1 and R_2 together with nitrogen and carbon atom to which they are attached respectively represent a 5 to 6 membered heterocyclic group,

- i) m is 1 or 2;
- ii) when m is 1, R is not fluorine and
- iii) when m is 2, the two substituents R are not both fluorine, or a pharmaceutically acceptable salt or solvate thereof.
- 80. (Previously Presented) The method according to claim 79, wherein said mammal is a human.
- 81. (Previously Presented) The method according to claim 79, further comprising administering an effective amount of a serotonin reuptake inhibitor.
- 82. (Currently Amended) The method according to claim 81, wherein said serotonin reuptake inhibitor is selected from the group consisting of fluoxetine, eiglepram citalogram, femoxetine, fluoxamine, paroxetine, indalpine, sertraline, zimeldine.
- 83. (Previously Presented) The method according to claim 79, further comprising administering an effective amount of a dopaminergic antidepressant.
- 84. (Previously Presented) The method according to claim 83, wherein said dopaminergic antidepressant is selected from the group consisting of buproprion and amineptine.
- 85. (Currently Amended) A method for the treatment of a panic disorder in a mammal comprising administering to said mammal an effective amount of a compound selected from the group consisting of 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;

19 of 31

- 2-(2-Isopropyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-Fluoro-3-methyl-phenyl)-piperazine-il-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2,4-Difluoro-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide;
- 2-(4-Fluoro-phenyl)- piperazine-1-carboxylic acid (3,4-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-Phenyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro-methyl-benzyl)-methyl-amide;
- 2-(3,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro-methyl-benzyl)-methyl-amide;
- 2-(4-Fluoro-2-methyl-phenyl)-3-methyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2-Methyl-4-Fluoro-phenyl)-6-Methyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phonyl) piperazine 1 carboxylic acid [1 (3,5-bis-trifluoromethyl-phonyl)ethyl]-methyl-amide;
- 4-(2-Amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(S)-(4-Fluoro-2-methyl-phenyl)-4-(piperidine 4-carbonyl) piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 4-(2-Amino-ethyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(1-3,5-bis-trifluoromethyl-phenyl)-cyclopropyl]-methyl-amide;
- [2-(3,5-Bis-trifluoromethyl-phenyl)-pyrrolidin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;

- [2-(3,5-Bis-trifluoromethyl-phenyl)-3,6-dihydro-*2H*-pyridyn-1-yl]-[2-(\$)-(4-fluoro-2-methyl-phenyl)-piperazin-[1-yl]-methanone;
- 2-(3,5-Bis-trifluoromethyl-phenyl)-piperidin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
- 2-(4-Fluoro-2-methyl-phenyl)-piperazine 1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-but-3-enyl] methyl-amide;
- 2-(4-Fluoro-2-methyl-phenyl)-piperazine-[1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propyl]-methyl-amide;
- 2-(4-Fluoro-2-methyl-phenyl)-piperazine-[1-carboxylic acid [(3,5-bis-trifluoromethyl-phenyl)-cyclopropy|-methyl]-methyl-amide; or an enantiomer, or pharmaceutically acceptable salt or solvate thereof.
- 86. (Previously Presented) The method according to claim 85, wherein said mammal is a human.
- 87. (Previously Presented) The method according to claim 85, further comprising administering an effective amount of a serotonin reuptake inhibitor.
- 88. (Currently Amended) The method according to claim 87, wherein said serotonin reuptake inhibitor is selected from the group consisting of fluoxetine, cialopram citalopram, femoxetine, fluoxamine, paroxetine, indalpine, sertraline, zimeldine.
- 89. (Previously Presented) The method according to claim 85, further comprising administering an effective amount of a dopaminergic antidepressant.
- 90. (Previously Presented) The method according to claim 89, wherein said dopaminergic antidepressant is selected from the group consisting of buproprion and amineptine.
- 91. (Cancelled.)

- 92. (Previously Presented) A method for the treatment of a panic disorder in a mammal comprising administering to said mammal an effective amount of 4-(2-Amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide hydrochloride.
- 93. (Currently Amended) A method for the treatment of a panic disorder in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phonyl) piperazine 1 carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phonyl)-ethyl] methyl amide 2-(4-fluoro-2-methyl-phonyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phonyl)ethyl]-methyl-amide or an enantiomer or pharmaceutically acceptable salt or solvate thereof.
- 94. (Previously Presented) A method for the treatment of a panic disorder in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide methansulphonate.
- 95. (Previously Presented) A method for the treatment of a panic disorder in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide acetate.
- 96. (Previously Presented) A method for the treatment of a gastrointestinal disorder in a mammal comprising administering to said mammal an effective amount of a compound of formula (I):

$$\begin{array}{c|c}
R_4 & N & R_5 \\
N & N & R_1 \\
N & R_{10} \\
R_{10} & R_{10}
\end{array}$$
(I)

wherein:

22 of 31

R is a halogen atom or a C_{1.4} alkyl group;

R₁ is hydrogen or a C₁₋₄ alkyl group;

 R_2 is hydrogen, a C_{1-4} alkyl, C_{2-6} alkenyl or a C_{3-7} cycloalkyl group; or R_1 and R_2 together with nitrogen and carbon atom to which they are attached respectively represent a 5-6 membered heterocyclic group;

R₃ is a trifluoromethyl, a C₁₋₄ alkyl, a C₁₋₄ alkoxy, a trifluoromethoxy or a halogen group;

 R_4 is hydrogen, a $(CH_2)_qR_7$ or a $(CH_2)_pCO(CH_2)_pR_7$ group;

 R_5 is hydrogen, a $C_{1,4}$ alkyl or a COR_6 group;

R₈ is hydrogen, hydroxy, amino, methylamino, dimethylamino a 5 membered heteroaryl group containing 1 to 3 heteroatoms selected from oxygen, sulphur and nitrogen or a 6 membered heteroaryl group containing 1 to 3 nitrogen atoms;

R₇ is hydrogen, hydroxy or NR₈R₉ wherein R₈ and R₉ represent independently hydrogen or C₁₋₄ alkyl optionally substituted by hydroxy or by amino;

 R_{10} is hydrogen, a C_{1-4} alkyl group or R_{10} together with R_2 represents a C_{3-7} cycloalkyl group;

m is zero or an integer from 1 to 3;

n is zero or an integer from 1 to 3;

both p and r are independently zero or an integer from 1 to 4;

q is an integer from 1 to 4;

provided that, when R₁ and R₂ together with nitrogen and carbon atom to which they are attached respectively represent a 5 to 6 membered heterocyclic group,

- i) m is 1 or 2;
- ii) when m is 1, R is not fluorine and
- iii) when m is 2, the two substituents R are not both fluorine, or a pharmaceutically acceptable salt or solvate thereof.

- 97. (Previously Presented) The method according to claim 96, wherein said mammal is a human.
- 98. (Previously Presented) The method according to claim 96, wherein said gastrointestinal disorder is irritable bowel syndrome.
- 99. (Previously Presented) The method according to claim 96, further comprising administering an effective amount of a 5HT3 antagonist.
- 100. (Previously Presented) The method according to claim 99, wherein said 5HT3 antagonist is selected from the group consisting of ondansetron, granisetron and metoclopramide.
- 101. (Currently Amended) A method for the treatment of a gastrointestinal disorder in a mammal comprising administering to said mammal an effective amount of a compound selected from the group consisting of
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2-Isopropyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-Fluoro-3-methyl-phenyl)-piperazine-il-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2,4-Difluoro-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide;
- 2-(4-Fluoro-phenyl)- piperazine-1-carboxylic acid (3,4-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-Phenyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro-methyl-benzyl)-methyl-amide;

- 2-(3,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro-methylbenzyl)-methyl-amide;
- 2-(4-Fluoro-2-methyl-phenyl)-3-methyl-piperazine-1-carboxylic acid (3,5-bistrifluoromethyl-benzyl)-methyl-amide;
- 2-(2-Methyl-4-Fluoro-phenyl)-6-Methyl-piperazine-1-carboxylic acid (3,5-bistrifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl) piperazine 1-carboxylic acid [1-(3,5-bistrifluoromethyl-phonyl)ethyl-mothyl amide;
- 4-(2-Amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(S)-(4-Fluoro-2-methyl-phonyl)-4 (piperidine 4-carbonyl)-piperazine-1carboxylic-acid (3,5-bis-trifluoromethyl-benzyl) methyl-amide;
- 4-(2-Amino-ethyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(1-3,5-bistrifluoromethyl-phenyl)-cyclopropyl]-methyl-amide;
- [2-(3,5-Bis-trifluoromethyl-phenyl)-pyrrolidin-1-yl]-[2-(S)-(4-fluoro-2-methylphenyl)-piperazin-1-yl]-methanone;
- [2-(3,5-Bis-trifluoromethyl-phenyl)-3,6-diflydro-2H-pyridyn-1-yl]-[2-(\$)-(4fluoro-2-methyl-phenyl)-piperazin-[1-yl]-methanone;
- 2-(3,5-Bis-trifluoromethyl-phenyl)-piperidin-1-yl]-[2-(S)-(4-fluoro-2-methylphenyl)-piperazin-1-yl]-methanone;
- 2-(4-Fluoro-2-methyl-phenyl)-piperazine 1-carboxylic acid [1-(3,5-bistrifluoromethyl-phenyl)-but-3-enyl]-methyl-amide;
- 2-(4-Fluoro-2-methyl-phenyl)-piperazine-il-carboxylic acid [1-(3,5-bistrifluoromethyl-phenyl)-2-methyl-propyl]-methyl-amide;
- 2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(3,5-bistrifluoromethyl-phenyl)-cyclopropyl-methyl]-methyl-amide; or an enantiomer, or pharmaceutically acceptable salt or solvate thereof.
- 102. (Previously Presented) The method according to claim 101, wherein said mammal is a human.

- 103. (Previously Presented) The method according to claim 101, wherein said gastrointestinal disorder is irritable bowel syndrome.
- 104. (Previously Presented) The method according to claim 101, further comprising administering an effective amount of a 5HT3 antagonist.
- 105. (Previously Presented) The method according to claim 104, wherein said 5HT3 antagonist is selected from ondansetron, granisetron and metoclopramide.
- 106. (Cancelled.)
- 107. (Previously Presented) A method for the treatment of a gastrointestinal disorder in a mammal comprising administering to said mammal an effective amount of 4-(2-Amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide hydrochloride.
- 108. (Currently Amended) A method for the treatment of a gastrointestinal disorder in a mammal comprising administering to said mammal an effective amount of 2 (S) (4 Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1 (R) (3,5 bis trifluoromethyl-phenyl) ethyl] methyl-amide 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide or an enantiomer or pharmaceutically acceptable salt or solvate thereof.
- 109. (Previously Presented) The method according to claim 108, wherein said gastrointestinal disorder is irritable bowel syndrome.
- 110. (Previously Presented) A method for the treatment of a gastrointestinal disorder in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-

- 1-carboxylic acid [1-(R)-(3,5-bis-trifluorornethyl-phenyl)-ethyl]-methyl-amide methansulphonate.
- 111. (Previously Presented) The method according to claim 110, wherein said gastrointestinal disorder is irritable bowel syndrome.
- 112. (Previously Presented) A method for the treatment of a gastrointestinal disorder in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluorornethyl-phenyl)-ethyl]-methyl-amide acetate.
- 113. (Previously Presented) The method according to claim 112, wherein said gastrointestinal disorder is irritable bowel syndrome.
- 114. (Currently Amended) 2-(S)-(1 Fluoro 2 mothyl-phenyl)piperazine-1-carboxylic acid [1-(R)-(3,5-bis trifluoromothyl-phenyl)-ethyl]methyl-amide 2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide or an enantiomer or
 pharmaceutically acceptable salt or solvate thereof.
- 115. (Previously Presented) The method according to claim 56, further comprising administering an effective amount of a serotonin reuptake inhibitor.
- 116. (Currently Amended) The method according to claim 115, wherein said serotonin reuptake inhibitor is selected from the group consisting of fluoxetine, cialopram citalopram, femoxetine, fluvoxamine, paroxetine, indalpine, sertraline, zimeldine.
- 117. (Previously Presented) The method according to claim 76, further comprising administering an effective amount of a serotonin reuptake inhibitor.

- 118. (Currently Amended) The method according to claim 117, wherein said serotonin reuptake inhibitoris selected from the group consisting of fluoxetine, sialopram citalopram, femoxetine, fluvoxamine, paroxetine, indalpine, sertraline, zimeldine.
- 119. (Previously Presented) The method according to claim 93, further comprising administering an effective amount of a serotonin reuptake inhibitor.
- **120**. (Currently Amended) The method according to claim 119, wherein said serotonin reuptake inhibitor is selected from the group consisting of fluoxetine, cialopram citalopram, femoxetine, fluvoxamine, paroxetine, indalpine, sertraline, zimeldine.
- 121. (Previously Presented) The pharmaceutical composition according to claim 34 further comprising a serotonin reuptake inhibitor.
- 122. (Currently Amended) The pharmaceutical composition according to claim 121, wherein said serotonin reuptake inhibitor is selected from the group consisting of fluoxetine, cialopram citalopram, femoxetine, fluvoxamine, paroxetine, indalpine, sertraline, zimeldine.
- 123. (Currently Amended) The pharmaceutical composition according to claim 34, wherein said compound of formula (I) is 2-(S) (4-Fluoro-2-methylphonyl) piperazine 1-carboxylic acid [1-(R) (3,5 bis trifluoromethyl-phonyl) ethylj-methyl-amide 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide or an enantiomer or pharmaceutically acceptable salt or solvate thereof.
- 124. (Previously Presented) The pharmaceutical composition according to claim 123, further comprising a serotonin reuptake inhibitor.
- 125. (Currently Amended) The pharmaceutical composition according to claim 124, wherein said serotonin reuplake inhibitor is selected from the

group consisting of fluoxetine, cialopram citalopram, femoxetine, fluvoxamine, paroxetine, indalpine, sertraline, zimeldine.

- 126. (Previously Presented) The pharmaceutical composition according to claim 34 further comprising a dopaminergic antidepressant.
- 127. (Previously Presented) The pharmaceutical composition according to claim 126, wherein said dopaminergic antidepressant is selected from the group consisting of buproprion and amineptine
- 128. (Currently Amended) The pharmaceutical composition according to claim 123 further comprising a seretorin reuptake inhibitor dopaminergic antidepressant.
- 129. (Currently Amended) The pharmaceutical composition according to claim 424 128, wherein said dopamine rgic antidepressant is selected from the group consisting of buproprion and amineptine